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to talk up the necessities and advantages of accurate birth registration. The prize which will be offered is a year's subscription to the Mothers' Magazine.

The Indiana State Board of Health is preparing a Mothers' Baby Book. It will be bound in cloth, and treats simply and briefly of the care of the baby. This book will be sent to every mother when her first child is born, together with a letter of congratulation from the board. The letter will have something to say regarding registration, and will therefore advance that particular feature.

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## PARALYSIS DURING ANTIRABIC TREATMENT.

### A REPORT OF TWO CASES IN WHICH PARALYSIS OCCURRED DURING THE COURSE OF ANTIRABIC TREATMENT.

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While the administration of the Pasteur antirabic treatment gives no serious complications or sequelæ in a large percentage of cases, there are occasional exceptions, which make it impossible to say that it is always harmless. Many persons who have taken the treatment complain of minor and vague symptoms, usually due to a neurotic element in the patient, which complaints can not be definitely attributed to the treatment.

However, there is one condition occasionally seen in these patients that seems to be the direct result of the treatment, viz, paralysis, more or less complete, and often sufficiently extensive to be a cause of anxiety as to the final result.

But few cases of this paralysis have been reported in America. Jones<sup>1</sup> reports two cases seen personally and adds reports of two others. Stimson<sup>2</sup> alludes to another case in 1910. At that time Stimson stated that about 76 cases with 4 deaths had been reported.

After searching the subsequent literature, I have found no cases reported, but in the reports on file at the Hygienic Laboratory from various Pasteur institutes that obtain virus from the Hygienic Laboratory and are under the supervision of their respective State and city boards of health, I find three cases of paralysis noted, the whole number of cases treated being 3,115.

In 1910 a report from California states, under heading of complications: "Paralysis, one case, very slight." In 1911 a report from Alabama states: "One case of paralysis, transient." In 1912 the North Carolina report says: "One patient developed paralysis on the

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<sup>1</sup> Jones: Journal American Medical Assn., 1909, vol. 53, p. 1625.

<sup>2</sup> Stimson: Facts and Problems of Rabies, Bulletin No. 63. U. S. Public Health and Marine Hospital Service, Washington, pp. 70-73.

fourteenth day of treatment. Diagnosed by several physicians as a typical case of anterior poliomyelitis."

The following two cases occurred in patients who were receiving the antirabic treatment at the Hygienic Laboratory of the United States Public Health Service:

CASE I.—C. W., age 34; white; male; occupation, policeman; weight, about 180 pounds.

*Family history.*—Both parents are living and in good health. The cause of death of the grandparents is uncertain, though all lived to old age, and the patient knows of no nervous, spinal, or mental disease in the family. Patient is married and has two normal, healthy children.

*Previous history.*—Had had the usual diseases of childhood, but since reaching adult age has never been sick enough to go to bed. There is no history of venereal disease, and patient states he has never used alcohol to excess. Has been on the police force for ten years and has been an officer of the bicycle squad for six years.

On July 8, 1913, he was bitten by a white setter dog of unknown ownership, which was running on the streets unmuzzled. The dog was killed and sent to the Bureau of Animal Industry, Department of Agriculture, where the presence of negri bodies was demonstrated.

The wounds consist of two small punctures on the middle finger of the right hand. The wounds were cauterized at the Casualty Hospital shortly after infliction.

On July 10 he began receiving the antirabic treatment at the Hygienic Laboratory. July 16. A slight local reaction at one site of injection is noted.

July 17. Moderate local reaction at two sites of injection.

July 18. Local reaction at sites of last two injections severe. There is considerable induration of the tissues in the immediate neighborhood of the injection sites.

July 19. Local reaction less marked. A moderate reaction is present at the sites of last two injections and is disappearing at those where first noted.

July 20. Slight local reaction present.

July 21. Slight local reaction present. After receiving the injection on this date he returned home and states that he felt tired and sluggish and lay down. Shortly afterward he felt nauseated and vomited a small amount of bile-stained fluid. He took a saline purgative, but vomited it in about two hours, and then tried another (citrate of magnesia) without effect. He noticed that his lower limbs felt heavy.

July 22. On arising he complained of pain in the abdomen and found that the coordination of the movements of the feet and legs was interfered with. He could walk with the aid of a cane, and he went to the laboratory by street car for his usual treatment. On the car he noticed that the jarring of the car while in motion accentuated the pain in the abdominal region. He reported at the laboratory about 10 a. m. He could walk with great difficulty, both feet dragging behind as he leaned forward on his cane, and laboriously drew each foot along until it was under the body. He complained of pain in the abdominal region, which seemed to extend around to the back. A superficial examination showed the knee reflexes were exaggerated and that sensation was present in the legs. The tongue was coated; temperature, 37.3° C. A specimen of blood was taken, and afterward examined for malarial parasites, with negative result. He was advised to return home and go to bed and remain quiet. He left for home in an automobile.

July 23. He was seen at his home at 11 a. m. by Dr. Barry, police surgeon, Asst. Surg. Leake, and myself. The patient states that he passed a restless night, and that he suffered considerable pain in the back and abdomen. Temperature, 39° C.; pulse, 80; respiration, 26. The local reaction at sites of injections is fading rapidly. He is unable to move the legs or toes voluntarily. The knee reflex is present, but

much lessened when compared with that of yesterday. Plantar reflex is present, and the reflex movement of the muscles causes pain. Babinski phenomenon not present. - Sensation to pain (pin point) present throughout lower limbs. Sensation to temperature impaired in feet and lower portion of legs. Last night he suffered from retention of urine, and was catheterized, and was again catheterized this morning at 11.30. About 18 ounces of clear urine were obtained. This was examined by Dr. Leake and found normal in every respect. Upper extremities are not involved. Respiration is of the costal type. A slight aortic murmur was detected by Dr. Barry, otherwise chest and contained organs seem normal. The chief subjective complaint is pain in the region of the abdomen and the lumbar spine.

July 24. Temperature, 37° C.; pulse, 60; respiration, 22. Sensation is unchanged from yesterday's condition. There is slight tenderness over the sciatic nerves. The patient states that light stroking of the skin of the legs and thighs produces an unpleasant sensation, hardly severe enough to be called pain, but firm pressure is not painful. The toes can be moved very slightly. The bladder and rectum are still paralyzed, though sphincteric tone is maintained. He perspires freely. Reflexes are all absent.

July 25. Temperature, 36.6° C.; pulse, 66; respiration, 18. The motor and sensory condition are unchanged. He states that the feet "felt as if asleep." The arms are not involved, and respiration is now diaphragmatic. The aortic murmur has disappeared.

July 26. Temperature, 37.8° C.; pulse, 72; respiration, 24. Condition practically that of yesterday.

July 27. Temperature, 37.2° C.; pulse, 76; respiration, 20. No change noticeable in patient's condition.

July 28. Temperature, 36.8° C.; pulse, 80; respiration, 22. There is slight improvement. He can move the toes slightly, and can voluntarily contract some of the muscles of the thigh, but not sufficiently to flex or extend any of the joints.

July 31. Improvement is slight, but noticeable. He can move the feet slightly in abduction and adduction, but flexion and extension of the ankles can not be obtained. He can turn himself in bed quite readily. Bladder and rectal condition unchanged. Normal urination is not reestablished, but he feels a strong desire to urinate when the bladder is full.

August 15. Normal urination reestablished and defecation is much easier.

August 17. He is able to sit up in a chair for a few minutes at a time and can sit nearly erect without pain in the back. The coordination of the movements of the feet is poor, but gradually improving; appetite is good, and he sleeps fairly well.

August 22. Since the last note improvement has been quite rapid. He is now able to sit up all day and can walk with the aid of a cane. On arising to walk he has to stand still for a few minutes before he takes the first step. He says he does this "to get the stiffness out" of his legs. The gait is somewhat spastic, each step ending with a sudden planting of the foot, with toe and heel striking the floor nearly at the same time. The rectum and bladder are working normally.

August 27. He is able to walk without a cane, and the gait is much more steady. His steps are slightly shorter than normal, and there is still some spasticity. Knee reflexes and ankle clonus are present and slightly exaggerated. He complains of a heavy feeling in the abdomen and has a tendency to constipation.

The management of the case during illness was left to Dr. Edmund Barry, police surgeon, who has kindly furnished me the following data regarding the treatment:

During the first few days bromides were given to allay restlessness. During the period in which catheterization was necessary hexamethylenamine, 5 to 7½ grains, was given three to four times a day.

In the early part of the illness strychnine,  $\frac{1}{30}$  grain three or four times a day, was administered, and this was gradually lessened to  $\frac{1}{60}$  grain thrice daily.

Several remedies were used in attempts to evacuate the bowels, including eserine hypodermically on two occasions, but none proved efficient except high rectal enemata.

In the later stages massage of the affected parts and electricity were employed, with good results.

The patient lost about 20 to 25 pounds in weight during the illness, but is rapidly recovering his loss since convalescence has become established.

The other case which has occurred in patients treated at this laboratory is the one alluded to by Stimson<sup>2</sup> in his *Facts and Problems of Rabies*, page 73.

The following data taken from the notes on the case on file at the laboratory will be of interest.

CASE II.—C. O. K., age 42, male, white.

This man handled and cared for his dog, cleansing its mouth; he does not remember having received scratches or wounds of any kind. There were a few slight abrasions on the hands when he applied for treatment. The animal was a collie shepherd dog owned by the patient. The dog was first noticed to be sick on May 8, 1909, and was pronounced rabid by Dr. Buckingham, veterinary surgeon.

*Previous history.*—At 8 years of age he had an attack of meningitis, which lasted three months.

*Present illness.*—On May 13 preventive inoculations were begun and discontinued on May 30. A moderate local reaction began on the sixth day, becoming less and less pronounced until the last day of treatment.

On June 1, 19 days after the beginning of the treatment, the patient's wife telephoned that the patient's hands and feet were paralyzed. He was seen by Drs. Stimson and Manning, who found the hands and feet slightly paralyzed and weak. There was some loss of sensation; knee jerks absent; pupils reacted to light.

June 3. Consultation of Drs. Stimson, Manning, Miller, Achucarro and Heinecke: Diagnosis of peripheral neuritis made; at this time condition about the same as on the previous day, with the addition of some pain or pressure over nerve trunks; occasional complaint of pain in back and head; no fever; light diet ordered.

June 4. Condition about the same. He complains of some difficulty in swallowing, and there is some accumulation of mucus in the trachea which is raised with difficulty. He slept little during the night.

June 5. Condition about the same.

June 8. Urine shows no sugar and but a mere trace of albumen.

June 10. Lips and eyes involved but has some control over them. He has some trouble with the palate in swallowing. The right arm is improved; can extend fingers and bring the hand to the face; sensation is also improved. Left hand also slightly improved; can extend the fingers and flex them slightly. He complained last night of intermittent pains in the arms and legs. The legs can be nearly completely extended without causing pain in the knees; he can not flex the legs; sensation in the hands is improved, especially in the right.

June 15. Has better use of the arms, and can close the eyelids. He can adduct the thighs but complains of pain when the legs are completely extended. His appetite is good.

June 18. The arms and face are much improved, having almost complete use of them. Legs are greatly improved, being able to flex, extend and adduct them. He

<sup>2</sup> Stimson: *Facts and Problems of Rabies*, Bulletin No. 65, United States Public Health and Marine-Hospital Service, Washington, pp. 70-73.

can move the feet. He still complains of pain on complete extension of the legs; referred to the knee. Face no longer flushed and appetite good.

There are no further notes in the second case, but I recently learned (August, 1913) that the man fully recovered after being confined to bed for 46 days.

There seems to be a difference of opinion among neurologists as to the exact lesion of this paralysis, some holding it is a myelitis, others that it is a neuritis. The first case described above seems to point toward an affection of the lower cord, while those in charge of the latter case seem inclined to consider the symptoms those of neuritis. The latter case showed an ascending paralysis which is described by most writers who have reported cases, but the former case did not ascend though we expected it would do so. Whether the fact that this patient had been riding a bicycle for several years, thereby using the lower extremities much and the upper extremities comparatively little, had anything to do with the extent of the paralysis is uncertain.

Concerning the pathogenesis of this paralysis there are numerous views, but considering its very infrequent occurrence, it seems apparent that individual susceptibility must play an important part in the causation of the trouble.

The chief theories as to the cause of the paralysis are as follows:

(a) That it is due to anaphylaxis resulting from the injection of foreign animal tissue (rabbits' cord);

(b) That it is due to a "toxin" elaborated by the specific organism of rabies;

(c) That it is due to rabies resulting from street virus received at the time the bite was inflicted;

(d) That it is due to rabies resulting from fixed-virus infection;

(e) That it is due to infection with extraneous organisms introduced with the virus during treatment;

(f) That it is due to hysteria and other neuro-psychologic disorders.

Of these theories, I believe the first mentioned has the most to recommend it, as in this, individual susceptibility undoubtedly plays the important part and is not open to objections which are applicable to the others.

In support of this theory it may be stated that paralysis is said not to have occurred where the dilution method of Höyges was used, which uses a much smaller amount of rabbit tissue than the original Pasteur method.

The comparative rarity of this sequel of the treatment is a strong argument against its being a fixed virus infection or due to a rabies toxin. The fact that it has occurred in cases treated in which the supposed infecting animal has subsequently been proven not to be rabid disposes of the street virus infection theory.

If due to extraneous microorganisms introduced with the treatment, said organisms are probably rare, as in the cases treated at the Hygienic Laboratory complications and sequelæ resulting from extraneous infection, such as abscesses, etc., have been practically nil.

That it is not due to hysteria seems indicated by its occurrence in patients who show no neurotic or hysterical tendencies in any way.

The occurrence of the paralysis may be explained as a manifestation of individual hypersusceptibility analogous to the comparatively rare cases showing untoward effects after the administration of diphtheria antitoxin.

It is hoped that physicians in general, and especially those connected with Pasteur institutes will report cases that may occur in their patients, so that a proper estimation of the frequency of this complication may be obtained. When a patient begins taking the Pasteur treatment one of the questions almost invariably asked is "Is there any harm done if the case is not infected with rabies?" or, "Are there any after effects of the treatment?" These questions are best answered by telling the percentage of cases showing any ill effects and letting the patient judge for himself. However, at present the percentage of cases is unknown. Taking into consideration the figures given by Jones <sup>1</sup> (7,080 treatments without a case of paralysis) and the 567 cases treated at the Hygienic Laboratory with 2 cases (0.35 per cent), it will be seen that the occurrence of paralysis is indeed a variable factor.

With rabies apparently increasing steadily among the canine population of the United States and a wider spread of knowledge of rabies the time is fast approaching when all physicians will be consulted regarding rabies and its treatment. It is the duty of those connected with this work at present to report serious complications and sequelæ, so that physicians in general may be able to give proper information and advice to those consulting them.

To do this it is necessary that all cases be reported as fully as possible.

After comparing European <sup>2</sup> and American figures, I find that the occurrence of this paralysis is about the same on both continents. However, the American figures that I have found do not cover all cases treated and possibly cases have occurred that have not been reported. If such is the case, it is to be hoped that those concerned will report their cases in order that all the data possible on this condition may be made available.

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<sup>1</sup> Jones: *Journal American Medical Assn.*, 1909, vol. 53, p. 1625.

<sup>2</sup> Remlinger: *Annal de l'Institut Pasteur*, 1905, Vol. XIX, p. 625. Pampoukis; *Deutsche Med. Wochenschrift*, 1908, Vol. XXXIV, p. 2076.